

## Reflections on Democracy, Science, and Cancer

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*The program at the December Stated Meeting opened with a tribute to Carl Cori, Visiting Professor of Biological Chemistry at the Harvard Medical School, on the occasion of his eightieth birthday. Severo Ochoa, Distinguished Member of the Roche Institute of Molecular Biology, reviewed Dr. Cori's scientific accomplishments, and Victor Weisskopf, President of the Academy, extended congratulations and best wishes on behalf of the membership. The communication of the evening was presented by Salvador Luria, Institute Professor of Biology at the Massachusetts Institute of Technology and Director of the Center for Cancer Research.*

One of the greatest surprises that I had when Carl and Anne Cori moved to Boston ten years ago was to discover not only that Carl spoke Italian (which is my maternal language) as well as I did, but also that his favorite poet in Italian, Giacomo Leopardi, was also mine, and that his favorite poem by that poet was my favorite. Therefore, I should like to preface this talk with my own translation of that poem which is called "L'Infinito":

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Always dear was to me this lovely hill  
And its tall hedge, that most of the horizon  
Conceals from view.

And sitting here and gazing,  
Unending space beyond that hedge I fathom  
And cosmic silence, and a quiet so deep  
My heart almost takes fright.

Yet, as I hear the wind storm through the  
branches,  
I match that voice to the infinite silence  
And think of time, and of the years gone by,  
And of the living present, and its voice.

Thus my thought drowns into infinity  
And sweet is drowning in that peaceful sea.

I think that with some stretching of the imagination this poem can provide a metaphor for the activity of a great scientist such as Professor

Cori: the duality between the infinite vistas of science and the deliberate concentration of activity on a chosen segment of that reality; the consonance of the thought of the scientist with the voice of the natural world; and, despite the instinctive fright that every scientist feels before the immensity of the natural world, the will to immerse oneself in that infinity.

The image of the hedge that shelters and screens away a major part of the horizon also provides a metaphor for the main topic of my talk which is the relation between the scientific enterprise and the society in which that enterprise is carried out. This relation has become increasingly complex and tense in the last two decades. The problems arise, I believe, from the internal stresses and contradictions both within society and within science.

Our society is fundamentally based on the premise of democracy. Modern democracy is the daughter of the rationalism of the seventeenth and eighteenth centuries and is therefore in a sense the twin sister of science. It is by its very origins committed to rationality, to optimism about the future of mankind, to faith in progress based on factual knowledge of the world. But at the same time western democracy is also committed to a utilitarian point of view, to a world of budgets and appropriations and cost-benefit accounting that puts a price on every item and on every activity. Thirdly, democracy is buffeted by a variety of irrational forces which range from the activities of the counter-cultures within our society, the persistence of economic injustice, and the aberration of war and nationalism, to racism and sectarian prejudices of all sorts.

The scientific enterprise itself also presents a multitude of facets. To its practitioners and to a certain number of initiated observers, science preserves the quality that made it, from Newton to Darwin to Einstein, the most daring and most successful adventure of the human mind. For the enthusiastic scientist, the scientific enterprise is a monument to humanity's intellectual power and freedom, the modern equivalent of the great

cathedrals that the burghers of the Middle Ages raised as monuments to their newly found sense of economic power and political freedom. But if science is the cathedral raised in praise of intellectual freedom, we must admit that too often, under the pressure of utilitarian society, the cathedral of science has come to look like one of those monasteries observed in the French countryside in which a modest church is almost hidden by a prosperous distillery. The sale of products becomes a justification for being allowed to pray to the Lord. It is a fact that science has become so expensive that its support can be justified only on the basis of the benefits that derive from it, which is to say that science has to be justified by the practical technologies that it generates. But unfortunately, the necessity to justify itself by the cost-benefit criterion has inevitably caused science to become involved in many of the national activities of society, a participation that in the long run is bound to undermine the rational heritage of science itself.

These multiple contradictions within both the enterprise of democracy and the enterprise of science are, I believe, at the root of the strains and misunderstandings that have arisen. I shall single out some of these problems and comment upon them in the rather restricted field of the biomedical sciences. The three aspects I shall discuss are, first, the cost-benefit reckoning of the fruits of research; second, the decision-making process in the selection of research programs; and third, the distrust of science and scientists that is manifested in our society at large and among certain elements of society in particular. Even though I cannot hope to come up with satisfactory practical solutions to these problems, I shall try to suggest possible steps for the restoration of confidence.

The cost-benefit problem is the one that most directly affects the pursuit of science. It manifests itself, for example, in the form of Congressional inquiries into whether the American public is getting its dollar's worth from the investment in research in terms of practical results, be these gadgets or vaccines or therapeutic ad-

vances. This is a perfectly legitimate request. After all, public money is appropriated for building distilleries, not to raise cathedrals. In order to carry out their work scientists have willingly accepted the practice of justifying the church by the distillery.

The main problem, however, is the misunderstanding that confuses basic research, from which come indirectly whatever benefits may be expected from science, with targeted research, which is nothing but the application of existing knowledge to a specific target. To carry the metaphor a step further, basic research on herbs and essences is what may ultimately yield a new heavenly liqueur; targeted research may succeed in producing a cheaper variety of Coca-Cola. The distinction between basic and targeted research is an extremely difficult one for the scientifically uneducated to grasp. There is an enormous difference between development research, which consists of the application of existing knowledge to a new target, and basic research, which means the creation of new knowledge that may or may not ultimately be relevant to a given problem. Sending a man to the moon involved nothing but Newtonian mechanics and considerable gadgetry. But to control cancer we must first understand what cancer is, how cancer cells behave, how cancer cells differ from normal cells and how normal cells are put together. The Newton of cancer has not yet appeared on the scene; perhaps he or she is completing graduate work at the present time.

Many kinds of answers have been given to the question of the cost-benefits derived from basic science. Dealing with biomedical science specifically, Benno Schmidt, former Chairman of the National Cancer Board, has pointed out that any serious industry would invest at least 5 percent of its budget in research, whereas the United States government, which spends \$110 billion for health activities, allocates only about \$3 billion for health-related research. This is but a pragmatic answer which does not take into account the difference between targeted and basic research. The total federal budget for research is

about \$25 billion of which over \$15 billion goes into a variety of war-related activities; nobody bothers or dares to ask many cost-benefit questions about those. All the attention is focused on the \$3 billion for biomedical science.

More convincingly, the Committee on the Impact of Biomedical Research has pointed out that most biomedical research deals with problems that are still unsolved at the basic level, that the benefits are indirect and sporadic, but when they come, they pay off handsomely in dollars for the investments that make them possible. The examples it gave were primarily from the field of immunology, including the eradication of poliomyelitis, of death due to Rh incompatibility, and soon, we hope, of infectious hepatitis. These are examples derived from only one area of biomedical science in which it can be demonstrated that the number of dollars in return are much greater than the number of dollars invested over a period of twenty or twenty-five years. This is really the crux of the matter.

New technology seldom if ever arises from the demand of an applied field. Discoveries that may lead to practical applications are made not because someone wanted to solve a practical problem but because many individuals were busy building their little corners of the cathedral. I'd like to quote from an article by our President, Victor Weisskopf, who himself was quoting H. B. Casimir:

"One might ask whether basic circuits in computers might have been found by people who wanted to build computers. As it happens, they were discovered by physicists dealing with the counting of nuclear particles because they were interested in nuclear physics.

... "One might ask even whether induction coils in motor cars might have been made by enterprises which wanted to make motor transport and whether then they would have stumbled on the laws of induction. But the laws of induction had been found by Faraday many decades before that.

"Or whether, in an urge to provide better communication, one might have found electromagnetic waves. They weren't found that way. They were found by Hertz, who emphasized

the beauty of physics and who based his work on the theoretical considerations of Maxwell. I think there is hardly any example of twentieth century innovation which is not indebted in this way to basic scientific thought."

In a more humble vein, let me describe my own experience as it relates to the cancer problem. In 1946 I was interested in a completely unapplied problem—the effect of radiation on genetic material. I asked myself whether a virus had one gene or many. (That would be a naive question today; we now know that some viruses have hundreds of genes, but in 1946 it was a perfectly legitimate inquiry.) Then I asked, if viruses have many genes, could two viruses be damaged by radiation in different genes in such a way that they might come together to reconstruct a good virus, that is, to repair each other. That curiosity led to the discovery that genetic material had a repair mechanism. Later it was found that all genes in all cells are subject not only to damage but to repair systems. But it took twenty years before someone found that the human disease, *Xeroderma Pigmentosum*, which is a frequent cause of cancers of the skin, is a genetic defect caused by an inability to carry out the repair of DNA injured by radiation. And only recently, ten years later, it is becoming apparent that the repair system present in every cell is error-prone; it makes mistakes as it corrects the damaged genes and these mistakes are mutations. It is likely that the cause of many of the cancers produced by chemicals is due to this malfunctioning of the gene repair system which we happened to stumble upon in our work in 1946. Just recently I heard of another example of a discovery leading to a practical application. A molecular biologist, who was studying the organization of actin filaments, the internal cellular skeleton in normal and cancer cells, made a discovery that appears to provide an early test for the hereditary disease known as familial polyposis of the colon, which is a frequent cause of a genetic cancer.

Let me suggest an analogy to the role of the basic scientist in the development of practical applications. The thousands of scientists work-

ing in their laboratories are like the uncountable numbers of coral polyps that are continually working under the waves, out of view, building immense coral reefs. The practical applications of science are like those rare sights when the coral reef emerges, forms an atoll on which a completely new set of life activities develop — birds, insects, plants, and mammals — using the new land created by the submarine work of the coral polyps but bearing little resemblance to the coral itself. Let us not forget that in the atoll itself, the coral polyps are usually dead.

A second area of concern for both science and the larger society is the decision-making machinery by which scientific priorities are chosen. In the scientist's view the problem seems to lie with the politicians; in the popular view, the problem is with the scientists themselves. Let me give an example. About six years ago the federal government became interested in a national cancer plan. Originally it was the brainchild of Mary Lasker and Sidney Farber; then it became a special project of Senator Yarborough; when he failed to be re-elected in Texas, Senator Kennedy assumed the leadership; and finally President Nixon adopted it as his own. After the President and Congress had made the decision, several hundred scientists were brought together to define and coordinate the research to be undertaken. Since 1972 the program has been quite successful in terms of scientific advances, yet it has already begun to come under attack by the cost-benefit advocates because in four years it has not yet solved the cancer problem.

The cancer program has been subjected to considerable criticism by scientists and the public. It was pointed out that cancer research was not, socially speaking, the most urgent area of need. Nutrition, child care, and many others seemed, to social reformers, to deserve primary attention. On the other hand, many scientists complained, not without reason, that the cancer program received a disproportionate share of the research funds and that basic research in other areas was suffering — which was true. And yet the cancer program, scientifically speaking, has

prospered. Why is this so? I think the answer is that it happened to be a field of biological research whose time had come, at least at the basic level.

In the past twenty-five years, molecular biology has made enormous advances relating to the nature of the gene, the genetic code, the nature of gene messages and their translation into the structure of proteins. These discoveries came about almost exclusively through work on bacteria and their viruses called bacteriophages. The next natural frontier was the cell of the complex organism, and here a completely new set of problems confronted the biologist. In bacteria every gene responds in a stereotyped way to changes in the extracellular environment, but in the varied types of cells in a complex organism, different sets of genes become programmed in development to function in specialized ways. Cells with identical genes *differentiate*. This is the central problem of development and the central problem of cancer as well. What makes a liver cell or a nerve cell or a skin cell what it is? How does a cancer cell behave the way it does?

It now appears that cancer cells and agents that cause cancers, including viruses, may be destined to play in the growth of molecular developmental biology the same role that bacteriophages played in the growth of molecular biology. Just as the orderly functioning of the genetic material of a bacterium could be explored by introducing into the bacterium a disrupting virus, so also the orderly functioning of normal cells may ultimately be clarified by studying what goes astray when a cell becomes cancerous. And in turn the growth of developmental biology may lead to the knowledge from which cancer prevention and therapy may evolve.

However, the fact that cancer research turned out to be a field whose time has come does not answer the criticism of the way it was chosen for priority. It is only because of the fundamental soundness of the scientific structure in this country and of the agencies that administer the program that a reasonable balance was achieved so that not much money was spent on trivial gad-

getry or on crash programs following untested leads.

The questioning of choices and priorities is only one aspect of a more diffuse phenomenon which may be defined as a crisis of confidence in the decision-making machinery of our society. This crisis of confidence is related, I believe, to the apparent inability of a successful society to manage large problems like the threat of atomic war and economic injustice — what I referred to as the irrationalities of our democratic life. More specifically, the crisis of confidence involves doubts as to the ability of society to handle intelligently and constructively the powerful technology that science has made possible. The contrast between the billion dollar spectaculars of NASA, the hundred billion dollar defense budgets, and the 25 percent unemployment among recent high school graduates — 35 percent if they happen to be black — does not increase public confidence in the effectiveness of our democracy to make rational choices and to provide for human needs. In the resulting frustration arises the third area of concern — the public distrust of science.

What is being questioned is usually the choice of priorities for research, as though scientists preferred to work on useless topics rather than useful ones. For example, Senator Javits, who has been a steady supporter of science in Congress, stated last April: "The decisions with respect to the future of biomedical research, the determination of priorities, the weighing of the non-quantifiable social costs and benefits of medical technology — these decisions are in fact political because they involve the entire body politic, including, of course, the research community itself. A scientist is no more trained to decide finally the moral and political implications of his or her work than the public — and its elected representatives — is trained to decide finally on scientific methodologies." This is a perfectly reasonable statement yet it fails to specify any clear or useful machinery by which scientists and the public can effectively cooperate in setting priorities. But the crisis of confidence goes beyond matters of priorities and choices. It questions the

*that faces  
scientists today*

*leads to*  
very integrity of scientists in the performance of their work, and it ~~can~~ cast them in the sinister light of the most lurid science fiction stories.

A ~~disturbing~~ example is the recent controversy surrounding recombinant DNA, a controversy that has been especially heated in Cambridge, *Mass.* The experiments that have elicited concern consist of joining together fragments of DNA from bacteria with fragments of DNA from cells of more complex organisms, plants or animals. The joined fragments can then be introduced into bacteria, grown in large amounts, and studied in a variety of ways to gain insight into the properties and functions of specific genes and groups of genes. This technology represents a powerful tool for the study of gene action and organization in complex organisms, and it will be a key for the molecular understanding of differentiation.

About two years ago the developers of this technology observed a self-imposed moratorium and called for national regulation in order to avoid the danger that genes from pathogenic organisms or cancer-producing viruses would be manipulated in this way, creating a hazard that was clearly foreseeable. Under prodding by these scientists who were exerting a welcome sense of responsibility, the National Institutes of Health formulated guidelines which stipulated that all potentially dangerous experiments, such as those involving genes of pathogenic viruses or even much less dangerous ones involving inhuman genes, can be carried out only in a few special laboratories under high containment conditions. Other experiments, including any in which genes of bacteria and of animals other than man are brought together, can be performed in less strict but still high containment laboratories under strictly controlled conditions.

Despite these safeguards, there has been strong criticism of all research involving recombinant DNA. The criticism falls into three categories which I would classify as mystical, sanitary, and political. I have very little patience with the first criticism; I believe the second is wrong, but I see some sound reason for the third.

What I call the mystical criticism is the assertion that there is something intrinsically wrong in creating new organisms by mixing the heredity of bacteria with that of complex organisms like plants or animals — the barriers that nature has set should not be crossed. In my view, there is not much point in arguing seriously against such an assertion. The argument of natural barriers to human knowledge has been put forward many times by the opponents of scientific progress, from the use of the telescope by Galileo to the use of steam engines to replace horse power.

The second type of opposition derives from a concern for safety. It is claimed that any organism carrying recombinant DNA may prove to be pathogenic and that therefore such experiments should not be done at all or done only in highly protected laboratories somewhere in the desert. Apart from the fact that there is no reason to suspect that genes from a plant or an animal should make a bacterium pathogenic for man (all bacteriologists know how difficult it is to cause any nonpathogenic bacterium to acquire pathogenicity), the simple answer to the question of safety is that the proposed experiments, innocent as they are in my opinion, will still be done under conditions of containment much stricter than those imposed on expert bacteriologists in hospitals or public health laboratories who are accustomed to handling true virulent pathogens.

The suggestion that the site of these experiments should be a remote laboratory which scientists could visit occasionally to carry out their work indicates a profound misunderstanding of the significance of this research. As I indicated earlier, the molecular study of differentiation is the current frontier of biology. Within this area the use of recombinant DNA techniques is not a peripheral technology which a scientist could perform once a month or once a year in a laboratory in the Nevada desert. It is a central methodology, as central as the use of a microscope. To tell the cell biologist today to forego recombinant DNA experiments would be like denying a chemist the use of nuclear magnetic resonants or a physicist the use of a laser. In my opinion, the

importance of recombinant DNA technology for basic biology definitely outsteps some of the practical applications that have been proposed, such as the mass production of insulin or of interferon.

On a more fundamental level it seems to me that attempts to put a limit on the scientific exploration of the human being by the most powerful means available, provided they are used responsibly, ignore the reality of today's world and of the world to come. As human beings we face problems that are not only technologically but biologically unique. To cope with the stresses and pressures that our own species will have to face in the next couple of centuries and to create a world fit for the new billions of human beings to live in, we shall have to understand as precisely as possible all interactions between our own body cells. We shall need to acquire a molecular understanding not only of vision but of the unique human brain, of human language, of human cognition. It is not through fear or distrust of experimental techniques that we shall acquire that knowledge. As Karl Popper stated in his Spencer Lecture, "Science and progress in science may be regarded as a means used by the human species to adapt itself to the environment."

And yet, while I disagree with the arguments put forward by the opponents of recombinant DNA research, I must admit that I feel some sympathy for the political implications of their opposition. Even though it is couched in sanitary or mystical terms, at least some of their criticism stems not ~~only~~ from distrust of science but from the political disaffection for what I called earlier the irrational elements of our society. It also represents a challenge to scientists and scholars to stand up as defenders of rationality against those irrationalities. Claims such as I have made — of the overriding human value of science, of its being a modern equivalent of the cathedrals of the Middle Ages — should be matched by evidence that scientists and other scholars are in fact selflessly dedicated to the cultural enterprise. Unfortunately, too often this is not true. Scien-

tists have lent their work and their prestige to what I consider some of the shabbiest enterprises of our society. To take only Vietnam as an example, some scientists and scholars have collaborated in all sorts of ways, from the weaponizing of the automated battlefield to the programming of the rain of fire over undefended villages to the planned uprooting of millions of innocent people. Vietnam is only one of the domains in which some scientists have gone along, passively or actively, with irrationality and the call of power.

What can be done to change this situation? In the first place, I think scientists should actively promote open discussion of the goals and limitations of science in order to generate an informed public consent that alone can give legitimacy to any social undertaking including science. But at a more fundamental level, I believe that what is needed to restore public confidence in the enterprise of science and the intellectual enterprise in general is for intellectuals and especially scientists to exert an active leadership in the restoration of rationality to our democratic society. Scientists should take the initiative in developing a common front with the public, not just to direct the uses of science to this or that goal of practical relevance but to help redirect the priorities of society itself away from irrationalities of social inequality or racial injustice or wanton waste or suicidal weaponizing. We cannot call ourselves the builders of today's cathedrals if we close ourselves into the cult of a private chapel or if we are willing to worship in the temples of Mammon. We cannot ignore or condone the irrational or inhuman uses to which the fruits of science are often put for reasons of power or profit. Only if scientists refused to join the ventures of injustice, if we refused to apply our knowledge to dehumanizing enterprises of society, if we insisted that the rationality in our work be matched by rationality in the uses to which the products of our work are placed, could we seriously claim to be the builders of a cathedral open to all for worship and wonder.